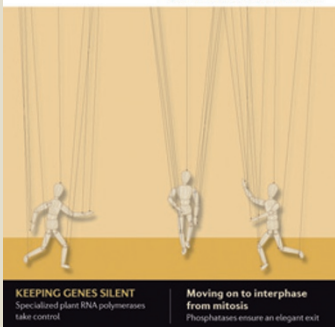




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► **COVER:** 'The invisible hand' by Vicky Summersby, inspired by the Review on p493.



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Cellular processes are controlled at many levels, from the action of regulators with global impact to the regulation of specific pathways or processes. On page 493, BurrIDGE and colleagues use the metaphor of an 'invisible hand' to describe how the RHO-specific guanine nucleotide dissociation inhibitors (RHOGDIs) operate behind the scenes to ensure the correct functioning of RHO GTPases, thereby affecting a broad range of cellular processes. They explore the mechanisms by which RHOGDIs function as regulators of RHO GTPases and discuss how RHOGDI–RHO GTPase interactions are themselves tightly regulated.

The uptake of material through clathrin-mediated endocytosis is another example of a broad regulatory mechanism. It affects processes such as signal transduction (by propagating or terminating signals) and cell–cell communication (for example, in synapses). On page 517, McMahan and Boucrot provide an overview of clathrin-mediated endocytosis, focusing on its modular nature, which allows it to adapt and fine-tune cargo selection.

Turning from a general mechanism of cellular control to one that operates at a specific time, on page 469 Wurzenberger and Gerlich discuss the key role of phosphatases in controlling mitotic exit. Safe passage through mitotic exit requires the organized removal of phosphates from many substrates and, in animal cells, it seems to rely on regulatory networks that involve the protein phosphatases PP1 and PP2A.

Also in this issue, Ana Maria Cuervo (page 535) presents a personal perspective and overview of the history of the discovery that lysosomes can selectively degrade cytosolic proteins — a process now known as chaperone-mediated autophagy. Many of the original ideas, which were initially controversial, were developed by J. Fred Dice, who sadly passed away last year.

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